EXHIBIT 4

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Environment and Health: Vital Intersection or Contested Territory?

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I. INTRODUCTION

The effects of environmental exposure, broadly defined as any exposure from outside the body, on human health are unquestionably the most important determinants of public health. While important genetic determinants of disease exert their effects irrespective of exposure from outside the body, these do not contribute as much to the overall public health burden of disease as factors such as tobacco smoke, poor quality water, inadequate or contaminated food, occupational exposures to dusts and chemicals, motor vehicle accidents, interpersonal violence, air pollution, and other factors external to the body.[1] In many cases, genetic predisposition and environmental exposures combined cause disease in an individual, so it may be impossible to separate out individual biological contributions from various external factors. Nevertheless, it is widely understood that public health concerns populations and communities, and that environmental determinants of health have been paramount throughout human history.[2]

Much of the scientific documentation of the impact of the environment on health has been produced in epidemiologic studies. The origins of the field of epidemiology are often traced to Dr. John Snow, who studied the patterns of cholera in London in the mid-nineteenth century.[3] His research, which included examining differential patterns of death in neighborhoods served by particular water companies,

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1 *See* THE GLOBAL BURDEN OF DISEASE: A COMPREHENSIVE ASSESSMENT OF MORTALITY AND DISABILITY FROM DISEASES, INJURIES, AND RISK FACTORS IN 1990 AND PROJECTED TO 2020 27 (Christopher J. L. Murray & Alan D. Lopez eds., 1996). This ongoing work ascribes the highest proportion of disease and disability to malnutrition, followed by poor water supply and poor sanitation.

2 *See* Francine A. Hochberg, Note, *HIV/AIDS and Blood Donation Policies: A Comparative Study of Public Health Policies and Individual Rights Norms*, 12 DUKE J. COMP & INT'L L. 231, 233 (2002).

3 For a detailed summary of Dr. Snow's research and contributions to epidemiology, see RALPH R. FRERICHS, JOHN SNOW, *at* http://www.ph.ucla.edu/epi/snow.html (last visited July 19, 2004).

hypothesizing a cause,[4] testing the hypothesis against alternative explanations, and recommending action to prevent community exposure to contaminated water, is still seen as a paradigm for modern public health practice.[5] While epidemiology is still considered the fundamental science of public health, and all schools of public health require students to take epidemiology courses,[6] in recent years there has been a tendency toward reductionist and individual-level explanations of disease causation.[7] Modern examples of the interplay between environmental toxic exposures and human health impacts abound,[8] but this Article focuses on the examples of childhood lead poisoning and cancer to illustrate the connections and controversies in this area of public health.

Furthermore, the relation between environmental exposures and disease has been the subject of lawsuits claiming harm from low-level toxic exposures to substances such as lead and synthetic chemicals.[9] These disputes are often sharply contested and occasionally break new legal ground.[10] In the last decade, the U.S. Supreme Court has attempted to provide guidance to the courts on how to handle scientific evidence in such cases, including *Daubert v. Merrell Dow Pharmaceuticals, Inc*.[11] This has led to some major obstacles for plaintiffs attempting to get their cases before juries in many parts of the United States.[12] The future of toxic tort litigation will rest, in part, on how the courts understand the scientific process and the evaluation of scientific literature, and how they interpret their "gate-keeping" role.[13] In this Article, we describe how epidemiologists draw

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4 Snow conducted his research before the germ theory of disease became the predominate causation theory. *See id*.

5 Peter F. Lake & Joel C. Epstein, *Modern Liability Rules and Policies Regarding College Student Alcohol Injuries: Reducing High-Risk Alcohol Use Through Norms of Shared Responsibility and Environmental Management*, 53 OKLA. L. REV. 611, 622 (2000).

6 *See* COUNCIL ON EDUCATION FOR PUBLIC HEALTH, ACCREDITATION CRITERIA: GRADUATE SCHOOLS OF PUBLIC HEALTH, *at* http://www.ceph.org (last updated June 2004).

7 *See* Neil Pearce, *Traditional Epidemiology, Modern Epidemiology, and Public Health*. 86 AM. J. PUBL. HEALTH 678 (1996). Pearce derides the narrowness of much "modern epidemiology" and calls for a return to the broad, population-based and action-oriented approach that gave the field its credibility.

8 *See* ENVIRONMENTAL TOXICANTS: HUMAN EXPOSURES AND THEIR HEALTH EFFECTS (Morton Lippmann ed., 2d ed. 2000)

9 *See*, *e.g.*, *In re* Agent Orange Prod. Liab. Litig., 611 F. Supp. 1223 (E.D.N.Y. 1985); City-Wide Coalition Against Childhood Lead Paint Poisoning v. Philadelphia Housing Authority, 356 F. Supp. 123 (D. Pa. 1973); Ecumenical Task Force of Niagara Frontier, Inc. v. Love Canal Area, 179 A.D.2d 261 (N.Y. App. Div. 1992).

10 *In re Agent Orange Prod. Liab. Litig.*, 611 F. Supp. at 1223.

11 509 U.S. 579, 589(1993); *see also* Kumho Tire Co., Ltd. v. Carmichael, 526 U.S. 137-147-50 (1999); General Electric Co. v. Joiner, 522 U.S. 136, 141-43 (1997). These three cases are sometimes called the *Daubert* trilogy and are the basis for the current judicial review of scientific evidence in toxic torts, especially at the Federal level, but in many State courts, as well. The full text of the *Daubert* decision and accompanying commentary can be found at http://www.defendingscience.org (last visited July 19, 2004).

12 *See* Jean Macchiaroli Eggen, *Toxic Torts, Causation, and Scientific Evidence After* Daubert, 55 U. PITT. L. REV. 889, 896 (1994) (discussing plaintiffs' difficulties of satisfying the preponderance of evidence standard in tort cases using scientific evidence); Michael H. Gottesman, *From Barefoot to* Daubert *to* Joiner*: Triple Play or Double Error*, 40 ARIZ L. REV. 753, 761 (1998) (indicating that in some jurisdictions, plaintiffs must provide evidence of causation to a high degree of certainty in order to avoid dismissal).

13 *See* Goebel v. Denver & Rio Grande W. R.R. Co. , 215 F.3d 1083, 1087 (10th Cir. 2000) ("It is within the discretion of the trial court to determine *how* to perform its gatekeeping function under *Daubert*.") (emphasis in original).

scientific inferences about causation and contrast this with post-*Daubert* tort practices.

II. CHILDHOOD LEAD POISONING: A CLASSIC ENVIRONMENTAL DISEASE

The earliest cases of childhood lead poisoning undoubtedly occurred many centuries ago. Lead pipes and pots were used for carrying water, cooking, preserving wine, and lead poisoning was recognized as a health hazard from the era of Hippocrates, approximately 400 B.C.[14] Subsequently, lead was a component of pottery glazes and other manufactured goods leading to periodic outbreaks of lead poisoning long before the modern era.[15] From a public health perspective, however, childhood lead poisoning has been reported as a widespread problem only in the past one hundred years or so.[16] The earliest cases were associated with ingestion of lead-based paint in homes and with the burning of lead batteries for fuel in poor communities during the winter.[17] In the United States, the first efforts to determine the full extent of the problem of childhood lead poisoning were in Baltimore, Maryland.[18] These early studies focused on the gross effects of high-level exposure and a condition called "plumbism," characterized by acute gastrointestinal symptoms, neurological symptoms such as seizures, and occasionally coma or even death.[19] Efforts to reduce exposure were focused on peeling paint in dilapidated inner-city housing and blood levels of clinical concern were reported in the medical literature.[20]

In the 1960s and 1970s, additional research showed that subtle effects, such as diminished IQ and behavioral and learning problems, were occurring at lower levels of exposure (see Appendix A).[21] This led to more intensive efforts to identify children at risk of these health effects, and a national plan to reduce childhood lead poisoning by eliminating lead-based paint for household use.[22] Unfortunately, a massive amount of lead was already present in the environment due to previous applications of lead paint and from exhaust from automobiles burning gasoline with lead additives[23]. Efforts to remove lead paint hazards from older housing were

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14 *See* Jerome O. Nriagu, *Historical Perspective on the Contamination of Food and Beverages with Lead*, *in* DIETARY AND ENVIRONMENTAL LEAD: HUMAN HEALTH EFFECTS 1, 1-4 (Kathryn R. Mahaffey ed., 1985).

15 *Id.* at 30-31.

16 Jane S. Lin-Fu, *Historical Perspective on Health Effects of Lead*, *in* DIETARY AND ENVIRONMENTAL LEAD: HUMAN HEALTH EFFECTS 51, 51-52 (Kathryn R. Mahaffey ed., 1985).

17 *Id.* at 52-55.

18 J. Julian Chisolm, Jr. et al., *Dose-Effect and Dose-Response Relationship for Lead in Children*, 87 J. PEDIATRICS 1152 (1975).

19 *Id.*

20 *Id.*

21 H. L. Needleman et al., *Deficits in Psychologic and Classroom Performance of Children With Elevated Dentine Lead Levels*, 300 NEW ENG. J. MED. 689, 694 (1979). Dr. Needleman and colleagues have been at the forefront in identifying health and behavioral consequences of childhood lead exposure. The current assessment is that there is no safe threshold below which there are no adverse effects. *Id.*

22 CENTER FOR DISEASE CONTROL, U.S. DEPARTMENT OF HEALTH, EDUCATION AND WELFARE, PREVENTING LEAD POISONING IN YOUNG CHILDREN (1978), *available at* http://www.cdc.gov/nceh/lead/publications/pub_Reas.htm.

23 CENTERS FOR DISEASE CONTROL AND PREVENTION, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, PREVENTING LEAD POISONING IN YOUNG CHILDREN ch. 3 (1991), *available at*

minimally successful in the 1970s and 1980s,[24] and achieved only moderate gains in communities with additional sources of funds from federal agencies.[25]

In some states, such as Massachusetts and Maryland, local laws and state-level initiatives have led to more comprehensive childhood blood lead screening programs and abatement of lead paint hazards.[26] For example, Massachusetts has a very high estimated percentage of screening in high-risk communities and has removed or reduced lead paint hazards in thousands of dwellings where young children live.[27] This proactive approach resulted from the combined activities of pediatricians and primary healthcare providers, local and state health departments, and property owners.[28] This state-level program also provides for the training and licensing of lead paint removal workers and contractors.[29] The number of units inspected and where lead paint hazards have been abated has been impressive, but other states have been less aggressive and less successful over the past two decades.[30]

The second major source of lead in young children's environment has been leaded gasoline.[31] This source is equally widespread, although less concentrated than lead-based paint.[32] The history of the use of lead as an additive to reduce engine knock in automobile engines has been well documented,[33] and is an example of scientific information dismissed in the interests of promoting an industry. Concern about this source of childhood lead exposure compelled Congress to ban leaded gasoline in the 1970s under the Clean Air Act.[34] At about the same time, the Consumer Product Safety Commission severely restricted the amount of lead allowed in household paint.[35] Thus, in the 1970s the federal government likewise took aim at the two largest sources of lead in the United States. Since that time, the amount of lead in children's blood has steadily declined (see Appendix B) and is one of the clear cut examples of how regulatory action can have an immediate positive impact on children's exposure to an environmental hazard.

As more has been learned about the harmful effects of lead in developing children, the blood lead levels that are considered "undue lead absorption" have come down correspondingly. For example, the level of concern in the early 1970s was 40 micrograms per 100 milliliters of whole blood; the Centers for Disease Control and Prevention ("CDC") lowered this level to 30 micrograms per 100

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http://www.cdc.gov/nceh/lead/publications/books/plpyc/chapter3.htm [hereinafter CDC PREVENTING LEAD POISONING].

24 Cushing N. Dolbeare & Don Ryan, *Getting the Lead Out: Controlling Lead Paint Hazards in Housing* (Sept./Oct. 1997), *available at* http://www.nhi.org/online/issues/95/lead.html.

25 *See* Jane Schukoske, *The Evolving Paradigm of Laws on Lead-Based Paint: From Code Violation to Environmental Hazard*, 45 S.C. L. REV. 511, 545 (1994).

26 *See id.* at 527, 540-44.

27 MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH, CHILDHOOD LEAD POISONING PREVENTION PROGRAM, MASSACHUSETTS' FIGHT AGAINST LEAD POISONING: UPDATED TRENDS, 1993-1998 (1999), *available at* http://www.state.ma.us/dph/clppp/ledstats.htm#maps.

28 *Id.*

29 *Id.*

30 MARY JEAN BROWN ET AL., SMALL AREA ANALYSIS OF RISK FOR CHILDHOOD LEAD POISONING 4 (2001), *available at* http://www.afhh.org/res/res_publications.htm.

31 Henry Falk, *International Environmental Health for the Pediatrician: Case Study of Lead Poisoning*, 112 PEDIATRICS 259 (2003).

32 *Id.*

33 *See, e.g.*, David Rosner & Gerald Markowitz, *A "Gift of God"?: The Public Health Controversy over Leaded Gasoline During the 1920s*, 75 AM. J. PUB. HEALTH 344 (1985).

34 42 U.S.C. § 7545 (2000).

35 16 C.F.R. § 1303 (2003).

milliliters by the late 1970s, and eventually to 10 micrograms by the late 1990s.[36] Based on current knowledge, the CDC's position is that "no threshold has been determined regarding lead's harmful effects on children's learning or behavior."[37] In the late 1970s, the National Health and Nutrition Examination Survey estimated that 88.2% of children between the ages of one and five in the United States had blood lead levels greater than 10 mcg.[38] By the late 1980s, this survey indicated that the percentage of U.S. children with this blood lead level had declined to 8.6%.[39] The latest available survey data, from the years 1999-2000, indicates that this percentage is now 2.2%, or 434,000 children in the United States.[40] The 1991 public health goal for the nation of reducing to zero the number of children with blood lead levels greater than 25 micrograms by the year 2000 was not met, and the CDC has now set a new goal of reducing the number of children with levels greater than 10 micrograms by the year 2010.[41]

In conjunction with the increased knowledge about the sources and effects of lead on young children, legislation and judicial precedent have established legal remedies for victims of lead poisoning. For example, the Massachusetts statute[42] and associated regulations[43] provide for fines and civil actions to require property owners to remove lead paint hazards from homes where children under age six reside.[44] This law has been used for three decades to require de-leading, and occasionally has forced rental property owners to enter into consent decrees to make major renovations to deteriorating properties. In addition, attorneys have brought civil actions for damages to clients who were lead poisoned and have suffered neurological effects. The largest settlement of such a case in Massachusetts was announced in September 2003; the property management company agreed to pay $4 million to four individuals who had resided in a hazardous property in the mid-1980s and subsequently were unable to finish high school or get jobs.[45]

The lesson of childhood lead poisoning is largely one of unheeded early warnings,[46] followed by widespread adverse effects in children throughout the United States, and subsequent legal and regulatory steps to reduce the hazard many years later. The example serves as a cautionary tale in public health schools and

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36 CENTER FOR DISEASE CONTROL, U.S. DEPARTMENT OF HEALTH, EDUCATION & WELFARE, INCREASED LEAD ABSORPTION AND LEAD POISONING IN YOUNG CHILDREN (1975), *available at* http://www.cdc.gov/nceh/lead/publications/pub_Reas.htm.

37 Pamela A. Meyer et al., *Surveillance for Elevated Blood Lead Levels Among Children – United States, 1997-2001*, MORBIDITY & MORTALITY WEEKLY REP., Sept. 12, 2003, at 2.

38 *Id.* at 1.

39 CDC, DHHS, CHILDREN'S BLOOD LEVELS IN THE UNITED STATES, *at* http://www.cdc.gov/nceh/lead/research/kidsBLL.htm (last reviewed Mar. 12, 2003).

40 *Id.*

41 *Id.*

42 MASS. GEN. LAWS ch. 111, §§ 189A-199B (2003).

43 MASS. REGS. CODE tit. 105, § 460.080 (2001).

44 *See infra* notes 45-46 and accompanying text.

45 Azell Murphy Cavaan, *4 Win $4 Million in Paint Lawsuit*, REPUBLICAN, Sept. 16, 2003, at A1.

46 David Rosner & Gerald Markowitz, *Industry Challenges to the Principle of Prevention in Public Health: The Precautionary Principle in Historical Perspective*, 117 PUB. HEALTH REP. 501, 502-05 (2002).

literature, and the legal remedies may serve as a warning about future failures to act in time to prevent harm.[47]

III. ENVIRONMENTAL CANCER

The correlation of workplace and community exposures and increased cancer risk has been one of the most urgent environmental health issues of the past quarter century. In the United States, much of the concern has focused on toxic chemicals and radiation, both ionizing and non-ionizing, and their relationship to cancer clusters in communities, factories and sometimes schools. Citizens' organizations have focused on dramatic examples, such as incidents in Times Beach, Missouri[48] and Love Canal, New York,[49] both of which were evacuated because of community exposure to dioxin; others have learned from workplace experiences such as the Oak Ridge National Laboratory in Tennessee, where excess radiation has increased the risk of leukemia deaths in the workforce.[50] Similar concerns followed a disastrous explosion at a chemical plant in Seveso, Italy[51] and the nuclear power plant disaster in Chernobyl, Ukraine.[52] But numerous less-publicized examples have occurred in communities throughout North America, and healthcare and legal professionals are increasingly asked to evaluate the causes and consequences of these worrisome events for communities.[53] This Part addresses three aspects of the problem: the background of cancer incidence and mortality against which local clusters are assessed, the types of exposures which are known or suspected causes of such clusters, and the implications for healthcare or legal professionals who wish to provide guidance for concerned patients or communities.

A. UNDERSTANDING RECENT U.S. CANCER TRENDS

Over the past quarter century, the incidence of cancer in the United States has risen steadily, from an age-adjusted rate of 385 cancer diagnoses per 100,000 citizens in 1973 to 476 per 100,000 in 1999.[54] The age-adjusted cancer mortality rates in the United States increased during this period as well, yet have recently

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47 Current concerns about endocrine-disrupting chemicals and persistent organic pollutants have many of the earmarks of the lead paint and leaded gasoline stories of the past century. *See*, *e.g.*, Julie Wakefield, *Boys Won't Be Boys*, NEWSCIENTIST, June 29, 2002, at 42.

48 *See, e.g.*, Richard Clapp, *Environment and Health: 4. Cancer*, 163 CAN. MED. ASS'N J. 1009, 1009 (2000).

49 *See* ADELINE GORDON LEVINE, LOVE CANAL: SCIENCE, POLITICS AND PEOPLE (1982). Love Canal residents led a campaign to raise awareness about toxic threats to children's health that sparked a nationwide movement. *Id.* ch. 7, at 175.

50 *See* Steve Wing et al., *Mortality Among Workers at Oak Ridge National Laboratory: Evidence of Radiation Effects in Follow-Up Through 1984*, 265 JAMA 1397, 1399 (1991). This study was one of the first to show evidence of increased leukemia deaths in workers exposed to low-level ionizing radiation. *Id*.

51 *See* Pier Alberto Bertazzi et al., *Health Effects of Dioxin Exposure: A 20-Year Mortality Study*, 153 AM. J. EPIDEMIOLOGY 1031 (2001). This latest publication of the results shows increased deaths due to several malignant and nonmalignant diseases in those exposed to dioxin after the 1976 accident. *Id.*

52 *See* Denis Bard et al., *Chernobyl, 10 Years After: Health Consequences*, 19 EPIDEMIOLOGIC REVIEWS 187 (1997).

53 *See* E. Donald Elliott, *Planning and Managing Mass Toxic Tort Cases*, *in* ENVIRONMENTAL LITIGATION (Janet S. Kole & Larry D. Espel eds., 1991).

54 NATIONAL CANCER INSTITUTE, SEER CANCER STATISTICS REVIEW, 1973-2000 (L. A. G. Ries et al. eds., 2000), *available at* http://seer.cancer.gov/csr/1975_2000/sections.html.

declined largely because of improved treatments for some cancers and declining lung cancer mortality in males.[55] While there have been some improvements in the cancer patterns overall, it is instructive to examine some important trends in specific cancer types which may be due to avoidable exposures.

Table 1 shows the major types of cancer for which there are significant trends in both incidence and mortality.

Table 1: Cancer Types with Significant Trends in the United States, 1950-2000[56]

Cancers With Increasing Incidence and Mortality	Cancers With Decreasing Incidence and Mortality
Esophagus	Oral cavity and pharynx
Liver and intrahepatic bile ducts	Stomach
Pancreas	Rectum
Lung and bronchus	Cervix uteri
Melanoma of skin	Uterine corpus
Prostate	
Kidney and renal pelvis	
Brain and other nervous system	
Non-Hodgkin's lymphoma	
Multiple myeloma	
All sites combined	

The decreasing incidence and mortality from stomach cancer has been repeatedly noted, and has been associated with improved methods of storing and preserving food.[57] Likewise, the decreasing incidence and mortality due to cervical cancer is most likely the result of widespread screening efforts and early diagnosis and treatment.[58] On the other hand, cancers for which incidence and mortality continue to increase appear to be similarly avoidable. Lung cancer, particularly in females, non-Hodgkin's lymphoma, melanoma of the skin, multiple myeloma and several other, less common malignancies have continually increased.[59] Each of these seems to be largely the result of avoidable exposures. For instance, lung cancer is primarily due to exposure to cigarette smoke,[60] melanoma of the skin is strongly linked to frequent exposure to ultraviolet light,[61] and non-Hodgkin's lymphoma has been associated with environmental and occupational exposure to carcinogens.[62]

Considerable attention has been paid to the decline in mortality rates from some of the more common types of cancer in the United States over the past decade,

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55 *Id.*

56 *Id.* sec. 1, tbl. I-2.

57 *See Cancer Epidemiology: New U.K. Cancer Statistics Released for Year 2000*, CANCER WEEKLY, Jan. 27, 2004, *available at* 2004 WL 55262873.

58 *Gynecological Cancer: Proteomics is the Newest, Most Promising Direction for Gynecologic Cancer*, CANCER WEEKLY, Jan. 6, 2004, *available at* 2004 WL 55262326.

59 NATIONAL CANCER INSTITUTE, *supra* note 54, at sec. 1, tbl. I-2.

60 *See Cancer Epidemiology: Global Cancer Rates Could Increase by 50% to 15 Million by 2020*, CANCER WEEKLY, Apr. 29, 2003, *available at* 2003 WL 9045477.

61 *See Skin Cancer: Sun Safety Alliance Discourages Sun Exposure for Vitamin D Deficiency*, CANCER WEEKLY, Apr. 20, 2004, *available at* 2004 WL 55265266.

62 *Cancer Incidence: Exposure to High Levels of Trichloroethylene May Increase Risk Of NHL*, CANCER WEEKLY, Feb. 10, 2004, *available at* 2004 WL 55263223.

including female breast cancer, prostate cancer in males, and lung and colorectal cancers in both sexes.[63] Between 1994 and 2000, the United States experienced a 0.3 to 1.4% annual decline in the age-adjusted cancer death rate for these cancers, which some observers attributed to reduced smoking in males and improved treatment of some cancers.[64] These declines are certainly good news for cancer patients, but considering the massive investment in cancer research and screening since the early 1970s, perhaps the most relevant observation is how little progress has been made in reducing cancer death rates.

Another measure of the national cancer burden is the estimated lifetime risk of being diagnosed with an invasive malignancy. This risk is periodically estimated by the National Cancer Institute's Surveillance, Epidemiology, and End Results ("SEER") program. SEER currently calculates this risk at 47% for males and 39% for females.[65] This means that nearly one out of two males will be diagnosed with invasive cancer, and four out of ten females diagnosed with some form of cancer in their lifetime. These estimates are significantly higher than the often-quoted cancer risk of "one in three." Although this increased lifetime risk partly reflects the overall aging of the U.S. population, it nevertheless implies increased suffering and distress for both cancer patients and their families. This reason alone is sufficient motivation to investigate ways to prevent cancer, along with the ongoing effort to improve treatment and supportive care.

B. Occupational and Environmental Causes of Cancer

Several authors have attempted to quantify the avoidable causes of cancer. In 1981, a widely-cited report by Sir Richard Doll and Richard Peto examined U.S. cancer deaths among white people under age sixty-five, and names tobacco products and dietary factors as the largest contributors to cancer mortality.[66] The proportion of cancer caused by occupational exposures and environmental pollution was comparatively slight.[67] A more recent report by the Harvard Center for Cancer Prevention revised these earlier estimates, but still suggested that 30% of total cancer deaths were due to tobacco and another 30% to adult diet or obesity.[68] By contrast, the study accorded only 5% of cancer deaths to occupational factors and a mere 2% to environmental pollution.[69] The accuracy of these estimates is open to question, but it is not productive to trivialize or diminish a particular avoidable cause simply because it does not equal the large impact of a well-known culprit like tobacco on the overall cancer burden. Clearly, some factors interact and magnify the

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63 *See* Hannah K. Weir et al., *Annual Report to the Nation on the Status of Cancer, 1975–2000, Featuring the Uses of Surveillance Data for Cancer Prevention and Control*, 95 J. Nat'l Cancer Inst. 1276 (2003).

64 *See* Philip Cole & Brad Rodu, *Declining Cancer Mortality in the United States*, 78 Cancer 2045 (1996).

65 *See* National Cancer Institute, *supra* note 54, at sec. 1, tbl. I-15.

66 Richard Doll & Richard Peto, *The Causes of Cancer: Quantitative Estimates of Avoidable Risks of Cancer in the United States Today*, 66 J. Nat'l Cancer Inst. 1191 (1981). This was the first major attempt to quantify the factors which contribute to cancer deaths in the United States and was cited for many years, even though it is restricted to white deaths under age sixty-five, or less than half of the total cancer deaths.

67 *Id.*

68 Harvard Center for Cancer Prevention, *Harvard Report on Cancer Prevention*, 7 Cancer Causes Control S1 (1996). This analysis attempted to update the Doll and Peto analysis with more recent studies.

69 *Id.*

effect of each acting separately: asbestos and tobacco smoke in workplaces,[70] or tobacco smoke and radon in homes are two examples of such synergistic exposures[71]. The goal, then, should be to reduce all avoidable cancer risks wherever and whenever the opportunity arises.

Melanoma of the skin and non-Hodgkin's lymphoma have both been increasing rapidly over the past two or three decades; both of these are significantly linked to environmental and occupational exposures, such as ultraviolet light[72] or chemical solvents,[73] in addition to inherited predisposition.[74] The International Agency for Research on Cancer ("IARC") has listed two dozen individual agents, summarized in Table 2 below, known to cause cancer in humans.

Table 2: Some Established Occupational and Environmental Carcinogens[75]

Exposure	Target Organ in Humans
Aflatoxins	Liver
4 - Aminobiphenyl	Bladder
Arsenic	Lung, Skin
Asbestos	Lung, Pleura, Peritoneum
Benzene	Hematopoietic system
Benzidine	Bladder
Beryllium	Lung
Bis(chloromethyl)ether	Lung
Cadmium	Lung
Coal-tar pitches	Skin, Lung, Bladder
Erionite	Pleura
Mineral oils	Skin
Mustard gas	Pharynx, Lung
2 – Naphthylamine	Bladder
Nickel compounds	Nasal cavity, Lung
Radon	Lung
Shale oils	Skin
Silica	Lung
Solar radiation	Skin
Soots	Skin, Lung
Talc containing asbestiform fibers	Lung
2,3,7,8 – Tetrachloro-dibenzo-p-dioxin	Lung, Soft tissue sarcoma
Tobacco smoke	Lung, Bladder, Oral cavity, Pharynx, Larynx, Esophagus
Vinyl chloride	Liver, Lung, Blood vessels

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70 *See* Paul B. Lipsky et al., *Red Snapper or Crab?*, 350 NEW ENG. J. MED. 1443 (2004).

71 *See* Ragner Rylander, *Environmental Tobacco Smoke And Lung Cancer*, 323 NEW ENG. J. MED. 834 (1990).

72 Barbara A. Gilchrest et al., *The Pathogenesis of Melanoma Induced by Ultraviolet Light*, 340 NEW ENG. J. MED. 1341 (1999).

73 *See* Paul A. Scherr & Nancy E. Mueller, *Non-Hodgkin's Lymphomas*, *in* CANCER EPIDEMIOLOGY AND PREVENTION (David Schottenfeld & Joseph F. Fraumeni, Jr. eds., 2d ed. 1996).

74 *Id.*

75 *See* INTERNATIONAL AGENCY FOR RESEARCH ON CANCER, OVERALL EVALUATIONS OF CARCINOGENICITY TO HUMANS, *at* http://193.51.164.11/monoeval/crthgr01.html (last updated July 7, 2004).

IARC has considerably expanded this list of known human carcinogens over the past thirty years, as research studies have fortified scientists' knowledge about the human health effects of various chemicals, drugs, and other environmental and occupational exposures.[76] Scientists are currently evaluating other potential carcinogens which may pose a major public health risk for industrialized nations, including electric and magnetic fields and environmental estrogens.[77]

C. IMPLICATIONS FOR CANCER PREVENTION

Much of the concern about environmental causes of cancer has arisen due to widely publicized events such as toxic pollution in communities containing industrial sites or radiation in those located in proximity to nuclear facilities. Many of these events are localized and the exposed population may be limited to the industrial workers or the communities immediately surrounding the facilities. Nevertheless, because exposed communities include children, infants, the elderly, and other sensitive populations, many community residents may be considerably more susceptible to effects from prolonged low-level exposure than are typical healthy adults. Newborns exposed to radioactive iodine, for example, are more likely to develop thyroid cancer than are adults with equivalent exposure.[78] This example and others demonstrate the importance of setting community exposure limits, through environmental regulation, below permissible adult workplace exposure limits for the same substance.

While recent downward trends in cancer mortality are gratifying, there are ongoing, yet avoidable, environmental and occupational exposures in many communities and workplaces. For example, the continuing problem of stratospheric ozone depletion means that exposure to ultraviolet radiation and the consequent risk of skin cancer will be a public health concern for decades to come.[79] Similarly, ongoing exposure to carcinogenic chemicals in the workplace must be minimized and safer substitutes must be found for many industrial materials. Rather than attempting to diminish such problems, or rank them below other cancer causes, it is in everyone's best interest to take environmental and occupational carcinogens seriously and seek opportunities to prevent further public exposure.

Toxic tort litigation has also been a mechanism for both resolving disputes between polluting companies or industries and individuals or communities who have been harmed. This approach has become more common in the past two decades, and has been popularized in books and movies in the past decade. The book and movie based on the experience of citizens in Woburn, Massachusetts, some of whom sought a verdict and civil damages award for the loss of children who died of leukemia, provided some insight into the difficulties surrounding such litigation.[80] In the past ten years, the Supreme Court decision in *Daubert v. Merrell-Dow* has

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76 *See id.*

77 *See* IARC, OESTROGENS, STEROIDAL, *at* http://193.51.164.11/htdocs/monographs/suppl7/oestrogenssteroidal.html (1987); IARC, STATIC AND EXTREMELY LOW-FREQUENCY (ELF) ELECTRIC AND MAGNETIC FIELDS (2002), *at* http://193.51.164.11/htdocs/monographs/vol80/80.html.

78 Ethel S. Gilbert et al., *Thyroid Cancer Rates and I-131 Doses from Nevada Atmospheric Nuclear Bomb Tests*, 90 J. NAT'L CANCER INST. 1654 (1998).

79 Frank de Gruijl & Jan van der Leun, *Environment and Health: 3, Ozone Depletion and Ultraviolet Radiation*, 163 CMAJ 851 (2000).

80 JONATHAN HARR, A CIVIL ACTION (1995).

further complicated matters for plaintiffs.[81] What follows is a summary of how epidemiologists evaluate scientific information and reach conclusions about causation in toxic torts.

IV. EPIDEMIOLOGY IN TOXIC TORTS

Epidemiologists concerned with the causes that contribute to human cancer risk routinely use the guidelines established by Sir Austin Bradford Hill, one of the twentieth century's leading statisticians, as a set of useful tools for drawing scientific inferences and deductions about causation from all the available relevant principles, data, information, and observations.[82] We present here a discussion of how epidemiologists inquire into the contributions of cancer-causing environmental exposures.

A. USE OF EXPERIMENTAL AND OBSERVATIONAL SCIENCES

Scientific practice explores more than questions of causation, but this is a central issue in many tort cases. What does "A causes B" mean to a scientist? Apart from philosophical aspects of scientific causality, most scientists have adopted a pragmatic approach whose formal articulation goes back at least to John Stuart Mill's famous "Method of Difference." [83] Briefly, Mill's Method holds that A causes B if, all else being held constant, a change in A is accompanied by a subsequent change in B.[84] The formal method to detect such an occurrence is the Experiment, whereby:

- all things are held constant except A and B,
- A is varied, and
- B observed.[85]

Not all sciences can use a strictly experimental method, however, and must make observations in the real world and deduce scientific facts by applying reasoning and principles from experimental sciences or logic and mathematics.[86] Geology and epidemiology are such sciences.[87] In one of the sub-disciplines of geology, seismology, scientists *observe* earthquakes;[88] they certainly do not stage city-sized experiments on the factors that cause earthquakes. The inability of geology or astronomy to conduct full-scale experiments does not connote an inability to conduct good science, or that the science involved is inherently more

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81 Daubert v. Merrell Dow Pharm., Inc., 509 U.S. 579 (1993).

82 The historical context of these guidelines is of interest: Sir Bradford Hill proposed his viewpoints in 1965, well before the International Agency for Research on Cancer ("IARC") or U.S. agencies, such as the Environmental Protection Agency or Occupational Safety and Health Administration, had begun promulgating lists and categories of carcinogens. Further, Dr. Bradford Hill's own commentary on the use of his guidelines was most instructive; they are not meant to replace common sense and judgment but to aid them. Hill's viewpoints are further discussed in Part IV.B. of this Article.

83 JOHN STUART MILL, SYSTEM OF LOGIC: RATIOCINATIVE AND INDUCTIVE (Longman, Green, & Co. 1906).

84 *Id.* at 373-426.

85 *Id.*

86 *Cf. id.* at 437-47.

87 *See* Linda A. Bailey et al., *Reference Guide on Epidemiology*, *in* REFERENCE MANUAL ON SCIENTIFIC EVIDENCE 121, 129 (1994).

88 *See* U.S. GEOLOGICAL SURVEY, INTRODUCTION TO SEISMOLOGY, *at* http://quake.wr.usgs.gov/research/seismology/ (last modified Nov. 26, 2001).

"error prone" or less reliable than a branch of science that can conduct full-scale experiments.[89]

Scientists may, however, extrapolate from laboratory scale experiments to make scientifically defensible statements about the origins of "dark energy" in space or the causes of earthquakes on our planet.[90] There may be disagreement among experts as to the aptness of a *particular* extrapolation or inference, but generally there is no disagreement that the process of applying events or principles observed on the scale of the laboratory bench to events occurring on the scale of a geographic region is scientifically defensible, and indeed something similar is the norm in virtually all observational sciences.[91]

In the biological sciences, in general, and in the public health field, in particular, inferences for one group of humans are regularly drawn from epidemiological studies from another group of humans.[92] Significantly, inferences about humans are also made on the basis of observations of, or laboratory experimentation on, animals.[93] Indeed, the scientific reasonableness of drawing inferences from animals to humans provides the principal justification for the decision of National Institutes of Health to devote hundreds of millions of dollars funds to animal research.[94] Any *particular* inference may be arguable, and certainly may be the basis of a dispute between the parties in a lawsuit, but the *method and reasoning* are not subject to debate.

In general there are three sources of information on the effects of toxic exposures in human beings: (1) case reports; (2) toxicological research, including both animal studies and chemical or structural research; and (3) epidemiological studies.

1. Use of Case Reports Regarding Human Beings

A case report in medical or scientific literature of a single case or series of cases is one of the most important sources of information scientists have regarding the effects of toxic substances on human beings. [95] Indeed, case reports are often the only source of such information. Detailed reports of cases of accidental poisonings or suicides provide information, such as autopsy data, biopsies, and detailed clinical data, not obtainable by any other route. Moreover they constitute important and obvious "natural experiments," experiments where the relationship between the exposure and effect is usually clear. The use of case reports in medicine is longstanding and important, as evidenced by the continued appearance of such reports in the literature.[96]

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89 *See* MILL, *supra* note 83, at 440.

90 *See id.* at 448-528.

91 *Id.* at 187.

92 MANUAL OF EPIDEMIOLOGY FOR DISTRICT HEALTH MANAGEMENT 9-10 (J. P. Vaughan & R. H. Morrow eds., 1989)

93 ENCYCLOPEDIA OF ANIMAL RIGHTS AND ANIMAL WELFARE (Marc Bekoff & Carron A. Meaney eds., 1998); NATIONAL HUMAN GENOME RESEARCH INSTITUTE, ABOUT THE HUMAN GENOME PROJECT, *at* http://www.genome.gov/10001772 (last updated June 2004).

94 PAWS N TAILS, ANIMAL TESTING–FACTS, *at* http://www.geocities.com/paws_n_tails/AnimalTestingFacts.html (last visited July 19, 2004).

95 For example, *The Lancet*, one of the world's leading medical journals, contains a Case Report every week. *See*, *e.g.*, Kathryn A. Tuohy et al., *Agitation by Sedation*, 361 LANCET 308 (2003).

96 MILL, *supra* note 83.

2. Use of Toxicological Studies

Toxicological research, including both animal studies and chemical or structural correlations, along with epidemiology, is another source of information that provides much of the basis for scientific judgments linking toxic exposures to health effects. Toxicology is an *experimental* science and the advantages of being able to conduct an experiment are obvious. Because John Stuart Mill's famous Method of Difference depends upon observing the result on B of a change in A, *other factors must be held constant*.[97] The essence of an experiment is the control of all factors, except for A and B.[98] This kind of control allows the scientist to ask quite precise questions about explicitly defined As and Bs, and obtain relatively unambiguous answers.[99]

3. Use of Epidemiological Studies

Epidemiological studies are observations of "natural experiments" that are occurring in the real world.[100] The idea is to find situations which are almost like laboratory experiments, observe them, obtain as much information as possible, and then interpret the results.[101] The essence of the natural experiment in epidemiology is almost always a comparison between groups; for example, a group exposed to a chemical and an unexposed group.[102] The ideal situation would be to have the groups in the real world the same or comparable in all relevant respects except for the variable under study. Unfortunately, such natural groupings are rarely comparable, and techniques must be used to account for known differences.[103] However, not all sources of non-comparability are known. If not a necessary accompaniment of the variable being investigated, these residual factors fall by chance in the two groups being compared. The result is that there are usually differences solely attributable to the random way these factors are distributed between groups in the particular study.[104] The "chance" fluctuations in apparently otherwise similar populations require an epidemiologist to use statistical tools to evaluate the role of "noise" that might be obscuring an underlying "signal."[105]

Observing unintended or "natural" experiments in the real world, which is the essence of observational sciences like epidemiology, has the enormous advantage that it involves human beings living under conditions similar to ones endured by plaintiffs in a personal injury suit. Nonetheless, questions inevitably arise about the biological and scientific comparability, and thus the legal relevance or "fit" of the people, exposures, and diseases studied in one place and time, and other people at other places and times. Questions such as whether the comparison of the cases and controls was truly comparing "like with like," are precisely the kind of problems that

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97 *See supra* notes 88-90 and accompanying text.

98 *Id.*

99 MILL, *supra* note 83, at 256.

100 *See generally* ANN ASCHENGRAU & GEORGE R. SEAGE, ESSENTIALS OF EPIDEMIOLOGY IN PUBLIC HEALTH (2003) (discussing the foundations of epidemiology in public health).

101 *Id.*

102 *Id.*

103 *Id.*

104 David Ozonoff, *Conceptions and Misconceptions About Human Health Impact Analysis*, 14 ENVTL. IMPACT ASSESSMENT REV. 499 (1994).

105 *See id.* at 506-10.

can be and generally are avoided in a tightly controlled experimental study.[106] Thus, as David Ozonoff explained in detail in a 1994 peer-reviewed article, toxicological experiments and epidemiological studies each have characteristic strengths and weaknesses.[107]

In view of the fact that different scientific disciplines have disparate strengths and weaknesses, and the propensity of scientists to disagree, the key question for scientists and courts becomes determining how scientists decide which studies, data, experiments, and articles to use and rely on, and for what purposes. In other words, how do they *interpret and apply* the results of scientific studies?

B. How Scientists Make Judgments About Causality

It is well known that when different scientists interpret the same studies they do not always reach the same conclusion. How and why do scientists interpret the "same" basic facts, the same set of numbers, the same research report, in different ways?

Two aspects and tools of scientific interpretation are relevant to this discussion. In the literature of scientific methodologies they are commonly (but not invariably) referred to as internal and external validity.[108] *Internal validity* refers to a judgment about the extent to which the experiment or study produces valid information on its own terms.[109] Thus, for internal validity the crucial question to be answered is not, "If benzene causes cancer in C57BL/6 mice, does it also do so in Wistar rats or humans?" but rather "Did the experiment validly show that benzene caused cancer in C57BL/6 mice?" *External validity*, on the other hand, refers to a judgment about the extent to which the internally valid results of an experiment or study can be generalized to other situations.[110] Thus, for external validity, the crucial question is not "Did the experimental evidence adequately demonstrate that benzene causes cancer in Wistar rats?" but rather "If benzene *does* cause cancer in Wistar rats, does it *also* do so in humans?"

At the heart of a case report, a toxicological experiment, or an epidemiologic study lies a comparison. Case reports usually call the attention of the medical community to an "interesting" observation, as compared with a previous or usual experience, such as a rare disease in the context of an unusual exposure.[111] In an experiment, the comparison is between the different states of B, when A is varied.[112] In an epidemiologic study, it is the analogous comparison in the "natural" or unintended experiment that is observed.[113]

Once an unusual event is observed, or an unexpected experimental result is obtained, it remains to explain or interpret the observation or result, whether it is a difference or a lack of a difference in the expected or compared entities.

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106 Marion K. Slack & Jolaine R. Draugalis, *Establishing the Internal and External Validity of Experimental Studies*, 58 Am. J. Health-System Pharmacy 2173 (2001).

107 Ozonoff, *supra* note 104.

108 *See* Slack & Draugalis, *supra* note 106.

109 David P. Farrington, *Assessing Systematic Evidence in Crime and Justice Methodological Concerns and Empirical Outcomes*, 587 Annals 49 (2003).

110 *Id.*

111 For instance, the sudden death of a worker exposed to hydrogen sulfide. Meg Godfrey, *Using PIDs in Confined Spaces*, 73 Occupational Health & Safety 40 (2004).

112 *See supra* notes 89-90 and accompanying text.

113 *See supra* notes 105-07 and accompanying text.

Take as an example a study comparing the health outcome of two distinct groups of human beings: one group comprised of factory workers who were exposed to a chemical used in the production process, and the other group consisting of all members of the general population, most (but perhaps not all) of whom were not exposed to the chemical. Suppose the workers have more disease than the general population.[114] There are three generic reasons such a difference, or lack thereof, might be observed, referred to as "bias," "chance," and real effect.[115] These factors are conceptually independent, but not mutually exclusive, forces.[116] That is, all or some of the forces can operate simultaneously. Each must be evaluated to extract a valid message ("the real picture" or "true signal") from the study.[117]

1. The Role of "Bias"

Another term for "bias" is "systematic error."[118] This differs somewhat from the common usage of the word, and in epidemiology the word has been refined and qualified to encompass a wide variety of sources of systematic error, each given a name.[119] For example, epidemiologists talk of various kinds of "information bias," such as "recall bias," "observation bias," or "differential or non-differential misclassification bias," as well as types of "selection bias" and "confounding bias".[120] All biases have as their underlying mechanisms factors that make the compared groups different in ways other than just the variable being studied.[121] Because the object of an experiment or study is to isolate one element (exposure to the chemical in my example), one must estimate the effect of the uncontrolled differences on the comparison.[122]

A common source of potential bias in an epidemiological study is "confounding," and we illustrate this with an example. Suppose scientists were comparing cancer rates in two groups. As in all epidemiological studies, this comparison is of the nature of an experiment, but one that is "handed to us" by nature, not one of our own devising. Thus, scientists are unable to control everything they might like in this comparison.[123] It might be, for example, that the workers in this hypothetical instance are considerably younger than the general population, and because cancer risks rise with age, they would be expected to have less cancer than the comparison group. If this difference were not somehow accounted for, the observed increase in the number or incidence of cancers in the worker group is actually likely to underestimate the true effect. The same non-comparability could influence a comparison in the opposite way if the workers were on average older than the general population.

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114 Note that the analysis works just as well in a case where there is no increased disease.

115 *See* U.S. ENVIRONMENTAL PROTECTION AGENCY, DIOXIN REASSESSMENT REVIEW, sec. 4.5.1, *at* http://www.epa.gov/sab/pdf/ec95021.pdf (Sept. 29, 1995).

116 *See id.*

117 *See id.*

118 *See*, *e.g.*, Bailey et al., *supra* note 87.

119 *Id.*

120 *Id.*

121 *Id.*

122 *Id.*

123 Epidemiologists often find that there are unanticipated problems or uncertainties in conducting epidemiologic studies, and that other epidemiologists usually are quick to point these out. As with most things, designing an informative study is difficult. Criticizing one is easy.

The most important means of coping with bias is to recognize it. An important part of the training and practice of an epidemiologist is to recognize and account for the effects of the inevitable non-comparability found in observational studies.[124] Once recognized, an epidemiologist can often gauge the impact of a source of bias on the results and adjust conclusions accordingly. Sometimes the data themselves can be "adjusted" or "controlled" to eliminate the non-comparability in the two groups for certain factors like age or sex.[125]

2. The Role of "Statistical Significance"

Not all sources of non-comparability are known.[126] Providing that they are not a necessary accompaniment of the variable being investigated, these residual factors are distributed by chance between the two groups being compared. The result is that there are usually differences solely attributable to the random way these factors are distributed between groups in the particular study. The "chance" fluctuations in apparently otherwise similar populations require an epidemiologist to use special tools to discern the true meaning from the chaos of disparate data—to see the true picture amidst a welter of images, or to hear the true, underlying "signal" in the midst of the noise produced by these variations.[127] The mathematical tools used for these purposes involve statistical analysis.[128]

The main purpose for statistics in epidemiology, then, is to evaluate the role that random effects or "chance" might have played in the results. Statistical methods *do not* prove that chance is the source of a difference, or lack thereof[129]. These methods only provide information on how likely it is that chance could have played a part if there were no bias and no true effect.[130] The meaning of "statistical significance" is that the likelihood that chance *could* have produced the observed results *if there were no bias and no real effect* is less than some arbitrarily predetermined level, such as 5% or $p<.05$.[131] It is not the same as an "error rate," as some have interpreted the *Daubert* decision to mean.[132]

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124 VICTOR J. SHOENBACH & WAYNE D. ROSAMOND, UNDERSTANDING THE FUNDAMENTALS OF EPIDEMIOLOGY: AN EVOLVING TEXT 13 (2000).

125 *Id.*

126 This is a deterministic view of disease causation. One could also take a probabilistic view, in which case scientists would have to discuss sample error from some assumed super-population of identical study settings. This alternative view does not affect any of the points made.

127 *Id.* at 49-50.

128 *Id.* at 50.

129 David Egilman et al., *Proving Causation: The Use and Abuse of Medical and Scientific Evidence Inside the Courtroom—An Epidemiologist's Critique of the Judicial Interpretation of the Daubert Ruling*, 58 FOOD DRUG L.J. 223, 237 (2003) ("Significance testing is a statistical technique used for evaluating the role of chance as a *possible* explanation for an observed association between cause and effect.") (emphasis added).

130 *See id.*

131 Troyen A. Brennan, *Causal Chains and Statistical Links: The Role of Scientific Uncertainty in Hazardous-Substance Litigation*, 73 CORNELL L. REV. 469, 505 (1988). The original source of the 5% criterion is lost in time. It apparently came from the original applications of statistical methods to agricultural experiments and expressed a cost-benefit statement about the expense of redoing a large trial involving a whole growing season and plots of various seeds and fertilizers. Its use for public health purposes might thus be questioned. It is interesting to note that in other sciences, notably, physics, another common criterion for "statistical significance" is not 5% but 10%. In any event, virtually every elementary statistics text warns the student of the highly arbitrary nature of the figure.

132 Barbara Frederick, Daubert v. Merrell Dow Pharmaceuticals, Inc.*: Method or Madness?*, 27 CONN. L. REV. 237, 241 n.27 (1994).

For the reasons stated above, it is absolutely false—and, indeed, a serious interpretive error—to assert that a result that is not "statistically significant" means the results must be due to chance and only to chance.[133] For these reasons, prominent epidemiologists eschew "statistical significance," believing that it is not a *sine qua non* of good science and maintaining that it is neither necessary nor appropriate as a requirement for drawing inferences from epidemiologic data.[134] These views are hardly new. Instead, they are representative of the views of both the statistician Hill, and some of most highly regarded epidemiologists in this country, such as Drs. Kenneth Rothman and Noel Weiss. Hill chided those who relied on "significance tests" to prove or disprove causation:

> No formal tests of significance can answer those questions. ("Is there any other way of explaining the set of facts before us, is there any other answer equally, or more, likely than cause and effect?") Such tests can, and should, remind us of the effects that the play of chance can create, and they will instruct us in the likely magnitude of those effects. Beyond that they contribute nothing to the 'proof' of our hypothesis." - "I wonder whether the pendulum, has not swung too far—not only with the attentive pupils, but with the statisticians themselves. - Fortunately I believe we have not yet gone so far as our friends in the USA where, I am told, some editors of journals will return an article because tests of significance have not been applied . . . ."[135]

Similarly, in an amicus brief to the Supreme Court in the *Daubert* case, Professors Rothman and Weiss stated: "Significance testing . . . is neither necessary nor appropriate as a requirement for drawing inferences from epidemiologic data."[136]

The amicus brief continued:

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133 Robert J. Lewis, Jr., *The Kansas Sentencing Guidelines Act*, 38 WASHBURN L.J. 327, 340 (1999).

134 Carl F. Cranor et al., *Judicial Boundary Drawing and the Need for Context-Sensitive Science in Toxic Torts After Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 16 VA. ENVTL. L.J. 1, 32-34 (1996).

135 Austin Bradford Hill, *The Environment and Disease—Association or Causation?*, 58 PROC. ROYAL SOC'Y MED. 296, 299 (1965).

136 Brief of Amici Curiae Kenneth Rothman et al. for Appellate, Daubert v. Merrell Dow Pharm., Inc., 509 U.S. 579 (1993) (No. 92-102).

> The notion that only when data demonstrate "statistical significance" do epidemiologists draw inferences about observed associations between suspected risk factors and medical conditions is mistaken. Significance testing is nothing more than a statistical technique that attempts to evaluate what is called "chance" as a possible explanation for a set of observations, and classify the observations "significant" or "not significant" based on the likelihood of observing them if there were no relationship between the suspected cause and effect. Testing for significance, however, is often mistaken for a sine qua non of scientific inference. . . . Scientific inference is the practice of evaluating theories. As such, it is a thoughtful process, requiring thoughtful evaluations of possible explanations for what is being observed. Significance testing, on the other hand, is merely a statistical tool that is frequently, but inappropriately, utilized in the process of developing inferences.[137]

Significance testing, in our opinion and in the view of many respected scientists, places too high a value on a "yes-no" answer to an oversimplified question: Is the probability that the observed association could appear by chance, even if there is no actual relationship, low enough to justify rejection of chance as the explanation of the observed association?[138] The result of using significance testing as the criterion for decision-making is that the focus is changed from the information presented by the observations themselves to conjecture about the role that chance could have played in bringing about those observations.[139] Dr. Rothman has stated the issue in the following way:

> With the focus on statistical significance, if chance seems to be a plausible explanation, then other theories are too readily discarded, regardless of how tenable they may be. As a result, effective new treatments have often been overlooked because their effects were judged to be "not significant," despite an indication of efficacy in the data. Conversely, if "significance" seekers find that the results of a study are calculated as improbable on the basis of chance, then chance is often rejected as an explanation when alternative explanations are even less tenable.[140]

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137 *Id.*

138 Egilman et al., *supra* note 129, at 237.

139 *See* Stephen E. Fienberg et al., *Understanding and Evaluating Statistical Evidence in Litigation*, 36 JURMETRICS J. 1, 21-23 (1995).

140 Brief of Amici Curiae Kenneth Rothman et al. for Appellate, Daubert v. Merrell Dow Pharm., Inc., 509 U.S. 579 (1993) (No. 92-102) (quoting Kenneth Rothman, *Significance Questing*, 105 ANNALS INTERNAL MED. 445, 445-46 (1986)) (citations omitted). According to the Rothman et al. amicus brief:

> A better approach to evaluating the error in scientific measurement is the use of "confidence intervals." A confidence interval is a range of possible values for a parameter that is consistent with the observed data within specified limits. The process of calculating a confidence interval within the chosen limits is know as "interval estimation."
>
> An important advantage of interval estimation is that it: "do[es] not require irrelevant null hypothesis to be set up nor [does it] force a decision about 'significance' to be made—the estimates can be presented and evaluated by statistical and other criteria, by the researcher or the reader. In addition the estimates of one investigation can be compared with others. While it is often the case that different measurements or methods

The outcomes of statistical tests are strongly influenced by the size of the study population. For small populations, very large observed differences, of substantial *public health* significance, may still not be *statistically* significant.[141] That is to say, a large effect that a scientist would take seriously from the public health point of view cannot be differentiated on its face from chance. Either chance or a real causal influence, or even bias, could be responsible for the worrisome effect. Conversely, in large populations, very slight and substantively meaningless differences can be "statistically significant."[142]

Statistical methods are sometimes viewed as standard, agreed-upon, and mechanical procedures.[143] Scientists even allow computers to do them, seemingly without human intervention.[144] But as any statistician knows, there is a great deal of judgment in deciding which tests to use in which circumstances, which tests are valid in those circumstances, and what they do and do not mean.[145] Less well recognized is that statistics itself is, like all active disciplines, a field in ferment and change. Thus not all statisticians will agree on the propriety of even commonly used tests.[146] In his recent book, *Statistical Inference*, Michael Oakes has written:

> It is a common complaint of the scientist that his subject is in a state of crisis, but it is comparatively rare to find an appreciation of the fact that the discipline of statistics is similarly strife-torn. The typical reader of statistics textbooks could be forgiven for thinking that the logic and role of statistical inference are unproblematic and that the acquisition of suitable significance-testing recipes is all that is required of him.[147]

> of investigation or theoretical approaches lead to 'different' results, this is not a disadvantage; these differences reflect important theoretical differences about the meaning of the research and the conclusions to be drawn from it. And it is precisely those differences which are obscured by simply reporting the significance level of the results."

Id. (quoting L. Atkins & D. Jarrett, *The Significance of "Significance Tests," in* DEMYSTIFYING SOCIAL STATISTICS (J. Irvine & I. Miles eds., 1979)).

141 A detailed example showing how results can be of public health significance but not statistical significance can be found in Ozonoff, *supra* note 104.

142 For example, a difference of one-eighth inch in height between East Coast children and West Coast children will be statistically significant if very large numbers of children on both coasts are measured.

143 *See* Colin Tapper, *Discovery in Modern Times: A Voyage Around the Common Law World*, 67 CHI.-KENT L. REV. 217, 241 (1991).

144 *Id*.

145 *See* Fienberg et al., *supra* note 139, at 14.

146 A good example is the Fisher Exact Test, commonly used for small tables frequently encountered in environmental epidemiology. Certain well known statistical programs even force the user to employ this test if several table cells contain expected values of less than five, even though it has been known for years that the test is inappropriate. *Cf.* Ralph B. D'Agostino et al., *The Appropriateness of Some Common Procedures for Testing the Equality of Two Independent Binomial Populations*, 42 AM. STATISTICIAN 198 (1988).

147 MICHAEL OAKES, STATISTICAL INFERENCE: A COMMENTARY FOR THE SOCIAL AND BEHAVIOURAL SCIENCES vii-viii (1986). Oakes then goes on to quote a review by Dusoir of a statistics text in a technical journal:

> A more fundamental criticism is that the book, as almost all other elementary statistics texts, presents statistics as if it were a body of coherent technical knowledge, like the principles of oscilloscope operation. In fact statistics is a collection of warring factions, with deep disagreements over fundamentals, and it seems dishonest not to point this out.

Id. at viii.

When used, statistical methods are meant to help scientists *evaluate* the possible role of chance.[148] However, scientists must also evaluate the possibility of a concurrent *real* effect separately, as we now discuss.

3. Assessing Whether a "Real Effect" is Present in a Research Study

The most important reason for a discrepancy between two study groups, however, is an actual effect or influence from the variable being studied (occupational exposure to a chemical, in my example); in other words, that "A *does* cause B." As discussed in greater detail below, scientists recognize that "causation" should not be regarded as an experimental or epidemiological result, but rather as a "*judgment*" made about the experimental or epidemiological data.[149]

It is apparently not always appreciated that this is true. There is a tendency to believe that somehow "causation" is not a subjective judgment or interpretation but an actual, real, objective, discoverable, and measurable property of a relationship that can be demonstrated empirically, as if some associations had readable labels on them that said "causal" and all scientists need, then, is the right instrument to read the label.[150] In sum, although some scientists may be loathe to admit it, and although many lawyers and judges may not believe it, there is simply no magic formula or easy checklist for making scientific judgments.[151]

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148 As expressed by the epidemiologist Kenneth Rothman in his *Daubert* amicus brief, "The result of using significance testing as a criterion for decision making is that the focus is changed from the information presented by the observations themselves to conjecture about the role chance *could* have played in bringing about those observations." Brief of Amici Curiae Kenneth Rothman et al. for Appellate, Daubert v. Merrell Dow Pharm., Inc., 509 U.S. 579 (1993) (No. 92-102) (emphasis in original). Kenneth Rothman is the author of a standard text, KENNETH ROTHMAN & SANDER GREENLAND, MODERN EPIDEMIOLOGY (2d ed. 1997), and the former Editor-in-Chief of the journal EPIDEMIOLOGY.

149 *See* REFERENCE MANUAL ON SCIENTIFIC EVIDENCE 157 (2000) ("causation is a judgment issue for epidemiologists and others interpreting the epidemiological data."); *see also* Kenneth Rothman & Sander Greenland, *Causation and Causal Inference*, *in* MODERN EPIDEMIOLOGY 7 (Kenneth Rothman & Sander Greenland eds., 2d ed. 1998). As professors Rothman and Greenland explain in their textbook:

> Perhaps the most important common thread that emerges from the debated philosophies [of scientific causation] is Hume's legacy that proof is impossible in empiric science. This simple fact is especially important to epidemiologists, who often face the criticism that proof is impossible in epidemiology, with the implication that it is possible in other scientific disciplines. Such criticism may stem from a view that experiments are the definitive source of scientific knowledge. Such a view is mistaken . . . . Even the most careful and detailed mechanistic dissection of individual events cannot provide more than associations . . . .

Id. at 22.

150 *See* Daubert v. Merrell Dow Pharm., Inc., 43 F.3d 1311, 1320 (9th Cir. 1995). Judge Kosinski, in the *Daubert* remand, writes of the plaintiff's case that it does not "attempt to show causation directly; instead, they rely on experts who present circumstantial proof of causation." *Id.* Of course there is no such thing as a "direct" proof of causation.

151 Professors Rothman and Greenland are not alone in their view that judgment—not a checklist—is a scientist's most useful tool in inferring causation. Indeed, that perspective is shared by a number of the nation's leading epidemiologists and other scientists, historians of science, and philosophers of science. Thus, an amicus brief tendered to the U.S. Supreme Court in the *Daubert* case by Harvard professors Stephen Jay Gould (Zoology, Geology, and History of Science, now deceased), Gerald Holton (Physics and History of Science), Everett Mendelsohn (History of Science), and Kathleen Joy Propert (Biostatistics), Columbia University professor Ronald Bayer (Sociomedical Sciences), and NYU professor Dorothy Nelkin (Sociology and Law) explained that "'[c]onclusiveness in inferring causality—in epidemiology as with the study of all free-living human beings—is a desire more often than an accomplishment.'" Brief of Amici Curiae Ronald Bayer et al. for Appellate,

C. UNDERSTANDING "NEGATIVE" STUDIES

Understanding the operation of bias and chance is especially important in interpreting so-called "negative studies," where no differences are apparent, or where the differences are not "statistically significant."[152] Differences produced by real effects can easily be masked by poor exposure classifications (misclassification bias), chance can appear as a possible explanation merely by virtue of a small population available for study (poor statistical power), and potential risks can be undetectable by observing the exposed population for too short a time (bias produced by failure to account for adequate latency).[153] On the other hand, factors that can produce spurious increases in exposed groups in occupational studies are much less common, as most forces operate to lower the observed risks, not raise them.[154]

A concluding statement is needed about how to interpret results of epidemiological studies with respect to causation. One of the most common "measures of effect" used in such studies is something called the Relative Risk ("RR"), or its close approximation, the Odds Ratio ("OR").[155] The RR is the risk in the exposed population divided by the risk in the unexposed population.[156] Thus, when RR = 2.0 the risk in the exposed population is double the risk in the unexposed.

The relative risks of cancers as revealed in many of the epidemiology studies of persons exposed to chemicals, such as benzene, beta naphthylamine, and mixtures of these and other substances, exceed 2.0.[157] To an epidemiologist using generally accepted methods of epidemiologic analysis, however, a RR of 2.0 or more is not necessary in order to show that a causal association is "more likely than not " present in the study population.[158]

In our experience as epidemiologists who participate in the legal process as experts, some attorneys maintain and some courts believe that a RR of 2.0 is needed before one can conclude from an epidemiological study that the outcome was "more

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Daubert v. Merrell Dow Pharm., Inc., 509 U.S. 579 (1993) (No. 92-102) (quoting Mervyn Susser, *Rules for Inference in Epidemiology*, 6 REGULATORY TOXICOLOGY & PHARMACOLOGY 116, 127 (1986)). These scholars went on to observe that "[a]s a consequence, those who seek in science the immutable truth they find lacking in the law are apt to be disappointed." *Id.* "One notable similarity [between law and epidemiology] is the dependence of both fields upon *subjective judgments*. . . . In the end, a quality which lawyers should understand—judiciousness—matters more than any. Scientists use both deductive and inductive inference to sustain the momentum of a continuing process of research. . . . The courts of law, and the courts of application, use inference to reach decisions about what action to take. Those decisions cannot rest on certitudes, most especially when population risks are converted into individual risks." *Id.* (quoting Susser, *supra*) (emphasis added).

152 EPA, *supra* note 115.

153 *Id.*

154 Of these, the most important are non-differential exposure misclassification and small sample size. *See* David Ozonoff, Assessing the Effects of Exposure Misclassification in Hazardous Waste Studies (1994) (paper presented at the annual meeting of the International Society of Environmental Epidemiology, Nov. 1994) (on file with author); *see also* David Ozonoff et al., *Health Problems Reported by Residents of a Neighborhood Contaminated by a Hazardous Waste Facility*, 11 AM. J. INDUS. MED. 581 (1987).

155 NATIONAL RESEARCH COUNCIL, ENVIRONMENTAL EPIDEMIOLOGY, VOLUME 2: USE OF THE GRAY LITERATURE AND OTHER DATA IN ENVIRONMENTAL EPIDEMIOLOGY 22 (1997).

156 *Id.*

157 DAUBERT: THE MOST INFLUENTIAL SUPREME COURT RULING YOU'VE NEVER HEARD OF (June 2003), *at* http://defendingscience.org.

158 *Id.*

likely than not" due to the exposure.[159] The arithmetic basis of this proposition would seem quite transparent,[160] but, like many things in this subtle and complex science, there are sound and accepted reasons why this argument is not valid.[161] The reasons are both technical and ethical.

The RR, or its equivalent, the OR, as an estimate of the RR, is itself an estimate from the data of an underlying reality, the "real" risk.[162] RRs or ORs, like other statistics used to summarize data, have some margin of uncertainty associated with the fact that the data are, in some sense, just one realization of an idealized, very large set of possible realizations; just as the results of flipping a fair coin ten times varies from one realization, or set of ten flips, to the next. Thus, the RR or OR has a "confidence interval" around it that expresses how "stable" the estimate is in repeated trials[163]. A 95% confidence interval is the range of numbers that would include the "real" risk 95 times out of 100 if the same study were done over and over again, allowing for random fluctuations of the data inherent in the selection of subjects. Thus, a RR of 1.8 with a confidence interval of 1.3 to 2.9 could very likely represent a true RR of greater than 2.0, and as high as 2.9 in 95 out of 100 repeated trials.

A RR of 1.9 is a summary of the overall risk to a population that is usually heterogeneous with respect to important risk factors. Thus, it might include smokers, alcoholics, obese people, the elderly, persons who work in hazardous occupations, and persons who have other life conditions or life styles that may affect the risk of or susceptibility to particular toxins or diseases. If it turns out that a particular individual plaintiff with a disease has few or none of these risk factors, then a RR of 1.9 is a serious underestimate of the effects of his or her exposure. As age, smoking, weight, and other similar factors did not contribute to the development of the disease, they should not be used to discount the risk from exposure, as is done in an epidemiological study which "adjusts" for these factors.

This point has been made repeatedly in the literature, accompanied with graphic examples of how a study that produces a RR less than 2.0 could result from an exposure in which all of the cases, some of the cases, or none of the cases were the result of exposure. Without a specification of the underlying causation model, which in almost all cases is insufficiently known to allow an accurate calculation, or even any calculation, of the fraction of cases due to exposure, the doubling of the RR or OR is useless as a criterion for evidentiary admissibility.[164] The fact that it is sometimes used for this purpose has been described in the scientific literature as "a methodologic error that has become a social problem."[165] Here again, some courts

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159 *Id.*

160 If 1,000 cases appear "naturally" and another 1,000 are due to exposure (the result of a RR = 2.0), then of every 2,000 cases only 1,000 or 50% would seem to be a result of the exposure.

161 *See* Fienberg et al., *supra* note 139.

162 Bailey et al., *supra* note 87.

163 Ralph Metzger, *Epidemiology Can Be Your Friend: Using Epidemiology in the Courtroom*, *in* ATLA ANNUAL CONVENTION REFERENCE MATERIALS, VOLUME 2, 2815 (2001).

164 *See* Sander Greenland, *Relation of Probability of Causation to Relative Risk and Doubling Dose: A Methodologic Error That Has Become a Social Problem*, 89 AM. J. PUB. HEALTH 1166 (1999); Sander Greenland & James M. Robins, *Epidemiology, Justice and the Probability of Causation*, 40 JURIMETRICS J. 321 (2000).

165 For an illuminating comment, see Greenland, *supra* note 164. For a more extended discussion, see Greenland & Robins, *supra* note 164.

have interpreted the meaning of the *Daubert* decision as requiring a two-fold risk in an epidemiologic study before it can be relied upon by an expert.[166]

D. How Internal and External Validity of Studies is Evaluated

Evaluating internal validity requires the assessment of the roles played by bias, chance, and real effect.[167] Each can operate both to reinforce and offset other factors. There is often disagreement among experts, stemming from differing weights each places on the influence of bias, chance and real effect.[168] Such differences in science are common, both in and out of court. The fact that two scientists have different judgments about how much weight to give a study does not demonstrate that either has failed to use scientifically acceptable reasoning, but only that the ultimate opinion about the weight to accord a study is inherently part of the subjective judgment process of scientists.[169]

An evaluation of internal validity helps a scientist decide how much to rely on the specific results of a particular experiment or study. It does not tell a scientist how much to extend that result to contexts or situations different than the one studied in the particular study, or how much to generalize the result. Thus, a separate evaluation for *external* validity is needed.

Scientists observe and experiment in order to generalize; that is, to explain as much of the world as possible. Generalization is the source of science's fascination, power of explanation, and practical importance in the world outside the community of scientists. The limits and extent of the generalization that scientists can draw from a given study constitute the dimensions of the study's external validity.[170] For present purposes, the question is whether research results and conclusions developed in one context, such as a high-dose animal study, can be generalized to cover other contexts, including human exposures and disease.

Because there are no fixed, definite, and generally agreed upon rules about how—and how far—to generalize, each study must be evaluated in a specific context. Still, certain generic questions arise frequently, which we illustrate here with a brief example.

How does a scientist legitimately assert that a generalization that certain substances are likely to cause cancer in humans is valid and reliable? In essence, scientists put forth reasons why such a generalization makes sense, for example, that the animals involved are similar in pertinent respects to humans. This is followed by an examination of reasons that might limit the generalization, for example, that the high doses used may alter the process sufficiently that it no longer applies to human exposures.[171] Defining and constraining generalizations is an active process for forming opinions about studies. Again, there is ample scope for shades of opinion among experts who devote their professional time, resources, and best efforts to these areas of inquiry.

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166 *See*, *e.g.*, Marder v. G.D. Searle & Co., 630 F. Supp. 1087, 1092-93 (D. Md. 1986).

167 *See* Fienberg et al., *supra* note 139.

168 *See* DeLuca v. Merrell Dow Pharm., Inc., 922 F.2d 941 (3d Cir. 1990); State v. Sercey, 825 So.2d 959 (Fla. Dist. Ct. App. 2002).

169 *See* Eric D. Green et al., Problems, Cases, and Materials on Evidence 753-943 (3d ed. 2000).

170 *Id.*

171 It should be noted here that high-dose animal studies are generally accepted by scientists and regulators. *Cf.* J. E. Huff et al., *Carcinogenesis Studies: Results of 398 Experiments on 104 Chemicals from the U.S. National Toxicology Program*, 534 Annals N.Y. Acad. Sci. 1 (1988).

E. Developing an Opinion about the Scientific Information

Clinical observations and case reports, epidemiological and animal studies, and toxicological experiments are like pieces of a puzzle, albeit with the difference that the pieces are fit into a picture that is formed in the mind of the scientist. The scientist must also realize that some existing pieces may not fit, and thus may not be used, and that not all of the necessary pieces are available for placement when the scientist completes the process. Thus, fitting the pieces into a scientific picture is a fluid, dynamic, and difficult process.

Depending upon a scientist's judgment of the internal validity or inherent quality of a particular study, an individual "piece" may be clear and well defined, or fuzzy and indefinite. Depending upon a scientist's judgment of external validity of a particular study, he or she may decide that an individual piece forms a large and central part of the picture, is just a small piece on the periphery of the picture, or not part of the picture at all.[172] In addition, a scientist's experience, expertise and basic judgment are involved. The objective for the scientist, then, is to take the available puzzle pieces, judge their internal and external validity, and assemble a theory or working diagnosis. That is, to bring together the clear and definite and the most relevant pieces into a coherent, sensible, comprehensive, and "elegant" picture of "reality," a picture that represents the scientist's decision about "what is happening."[173]

Thus, a toxicologist studies cancer in the Zymbal gland in the rat and surmises that there is a mechanism whereby benzene produces damage in that species and which may or may not be relevant to other species, while an epidemiologist looks at cancer risks in human populations and concludes that benzene causes cancer in the human species. Each sees only a part of the picture.

As already noted, interpreting a scientific study for use in assembling a coherent picture requires the use of critical thinking to weigh the various factors that might be responsible for the observed association.[174] This includes evaluating the role played by bias, chance, and real effect, together and separately, and judgments on what generalizations are valid. In such a complex process and with practical matters of consequence at stake, it is not surprising that differences of opinion develop. It is also not surprising that such differences are highlighted and, indeed, magnified by the adversarial legal process. Even when so magnified, such disagreements are not merely *artifacts* of the adversarial process, or evidence of flawed scientific reasoning or methodology, but essential features of routinely practiced science.

In sum, scientists may, and often do, disagree about which pieces are internally and externally valid, and disagree about just how to assemble the internally and externally valid puzzle pieces. Indeed, most toxic tort litigation involves opposing scientific experts who sharply disagree about the relevance of the puzzle pieces, and how they fit together.[175] What scientists do not disagree about, though, is that they routinely select pieces and assemble such pictures and call the end product of this process an explanation.

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172 External and internal validity are thus analogous to the "reliability" and "fit" criteria of the *Daubert* Court. *See* Daubert v. Merrell Dow Pharm., Inc., 509 U.S. 579, 590-91 (1993).

173 *See* Robert R. Kuehn, *Suppression of Environmental Science*, 30 AM. J.L. & MED. 333 (2004).

174 *See infra* Parts IV.A-B.

175 *See*, *e.g.*, Kumho Tire Co., Ltd. v. Carmichael, 526 U.S. 137 (1999); Gen. Elec. Co. v. Joiner, 522 U.S. 136 (1997); Daubert v. Merrell Dow Pharm., Inc., 509 U.S. 579 (1993); Anderson v. W.R. Grace & Co., 628 F. Supp. 1219 (D. Mass. 1986).

V. CONCLUSION

The intersection of the environment and public health is unquestionably of critical importance and has been recognized for centuries. At the same time, this is often a highly contentious area of public health practice, especially when the economic stakes are high. Some of the most illuminating examples are the various effects of lead and other heavy metals on the health and development of children, including the difficulty in reducing exposure long after the harmful effects are known. Public health scientists faced strong opposition from automobile, lead paint and rental property interests when pressing for reductions in childhood lead exposure.[176] Similarly, many occupational and environmental chemicals are now known to cause cancer in humans, including some of the types of cancer that are increasing most rapidly in the United States. Nevertheless, scientists often dispute the contribution of these chemicals in the overall cancer burden and seek to minimize their importance.

In the legal arena, the evidence showing the effect of chemicals in causing cancer can be assembled from a variety of sources. Some victories have been won and have sent a message to the responsible parties, although the burden on plaintiffs has become heavier over the past decade. It is important to continue emphasizing that environmental exposures which cause childhood illnesses and cancer in both children and adults can be avoided. Informed citizens and their representatives can continue to advocate preventive policies and legal remedies. Pressure from these sources provides the best assurance that the mistakes that harmed public health in the past will not be repeated in the future.

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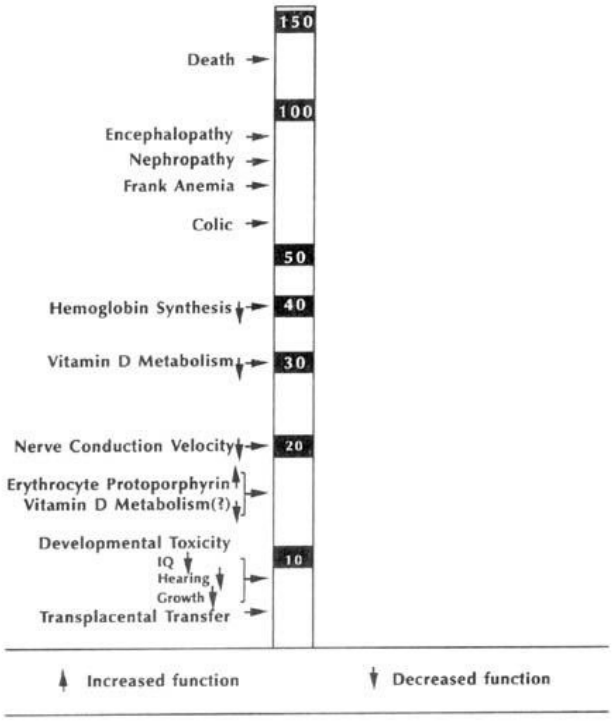
176 *See*, *e.g.*, Jennifer L. Bush, *The Federal Lead Poisoning Prevention Program: Inadequate Guidance for an Expeditious Solution*, 23 B.C. ENVTL. AFF. L. REV. 645 (1996); Robert A. Levy, *The New Business of Government Sponsored Litigation*, 9 KAN J. L. & PUB. POL'Y 592 (1994); Jane Schukoske, *The Evolving Paradigm of Laws on Lead-Based Paint*, 45 S.C. L. REV. 611 (1994).

APPENDIX A[177]

Figure 2-1. Lowest observed effect levels of inorganic lead in children*



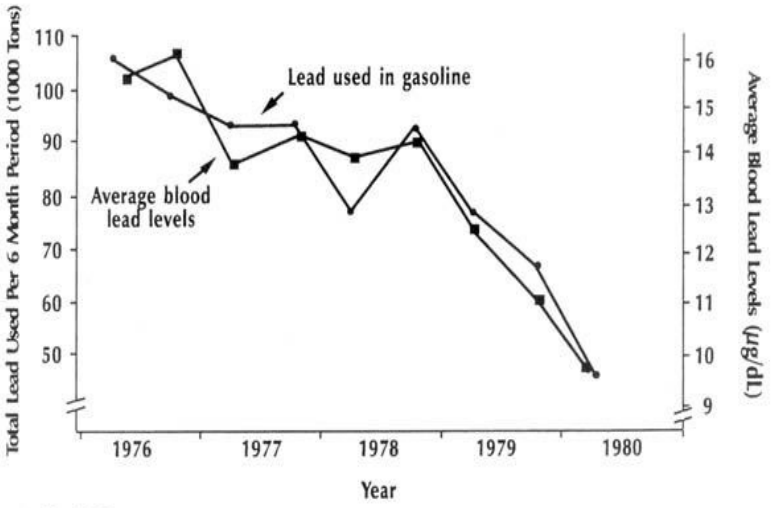
*Note: The levels in this diagram do not necessarily indicate the lowest levels at which lead exerts an effect. These are the levels at which studies have adequately demonstrated an effect.

Source: ATSDR, 1990.

177 AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY, CAC, CASE STUDIES IN ENVIRONMENTAL MEDICINE: LEAD TOXICITY, *at* http://www.atsdr.cdc.gov/HEC/CSEM/lead/index.html (last updated Aug. 20, 2003); *see also* CDC PREVENTING LEAD POISONING, *supra* note 23 (link to Figures).

APPENDIX B[178]

Figure 2-5. Change in blood lead levels in relation to a decline in use of leaded gasoline, 1976–1980



Source: Annest JL, 1983.

[178] J.L. Annest et al., *Chronological Trend in Blood Lead Levels Between 1976 and 1980*, 308 NEW ENG. J. MED. 1373 (1983).